# Exhibit 2

# Case 5:18-cr-00258-EJD Document 1098-3 Filed 10/18/21 Page 2 of 28

Message

From: Elizabeth Holmes [/O=THERANOS ORGANIZATION/OU=FIRST ADMINISTRATIVE

GROUP/CN=RECIPIENTS/CN=EHOLMES]

**Sent**: 10/11/2008 1:08:44 AM

To: Power, Aidan C Lipset, Craig

CC: Marc Thibonnier

Subject: RE: Follow up to our meeting

### Dear Aidan and Craig:

It is with great pleasure that I write to inform you we have now achieved our study goals.

In the interest of finishing as quickly as possible, we varied the enrollment schedules of some of our existing and new patients, as you will see in the attached.

Throughout this process, we have been compiling the data for our final report. I am very pleased to present you with the final data -- see the attached study report. We also have compiled all the raw data and included it for your reference in the attached spreadsheet. The report has been written in such a way that it could be circulated to people unfamiliar with Theranos.

Our 15 month study has validated the efficacy of our technology. We now have the foundation to apply it to

- 1) fast-tracking the approvals and label expansions of key therapies through generation of predictive and higher integrity data, faster and
- 2) significantly cutting costs to Pfizer's current study budgets by eliminating the need for sample shipments, overhead and analytical costs in the process.

The ability to profile protein time-courses in this way is allowing for predictive correlations to be extracted from biomarker measurements. One of our pharma partners quantified the impact of Theranos Systems accelerating time-to-market at \$1M a day after seeing correlations in a 6 month study that the conventional infrastructure took over 2 years to uncover. This work is on label expansion of an existing drug into a new indication; the ability to rapidly generate data on efficacy dynamics for market expansion has further implications for the revenue of the drug.

Since our meeting, we have cemented thoughts on the most powerful application of these systems for Pfizer. I wanted to wait until we received some highly anticipated return-on-investment data to share with you and we will now compile an overview of our systems and potential program(s) for you.

We have worked very hard on the angiogenesis program for a long time and are looking forward to translating our work into significant value creation for Pfizer.

Let us know if there is a convenient time next week for us to connect on this and next steps.

With my very best regards, Elizabeth.

Elizabeth Holmes President and CEO Theranos, Inc.



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# Case 5:18-cr-00258-EJD Document 1098-3 Filed 10/18/21 Page 3 of 28

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From: Power, Aidan C

**Sent:** Friday, August 22, 2008 10:00 AM **To:** Elizabeth Holmes; Lipset, Craig **Cc:** Marc Thibonnier; Stefan Hristu **Subject:** RE: Follow up to our meeting

Elizabeth - thank you for this. And thank you for hosting us on Tuesday. Aidan



# Theranos Angiogenesis Study Report

Prepared for Dr. Aidan Power Pfizer, Inc.

#### **Document Outline:**

- ∞ Introduction to Theranos
- ∞ Economic Impact of Theranos Systems to Pharma
- ∞ Angiogenesis Program Overview
  - o Study design
- - Specifications
  - Theranos System Performance
- ∞ Theranos Field Study
  - o Field Performance Overview
  - o Trial Data
  - o Evaluation of time course results from individual patients
  - Review of generated data, in aggregate by patient ID, sex, cancer type, treatment, etc.
  - Integrated patient information, including date and time of monitoring, medication received, self evaluation of overall health status of each patient and other clinical data in a comprehensive format
  - o Assessment of the technical performance of the Theranos System
    - Data transmission % success and mode of transmission used
    - General performance information as logged via the Customer Care line
    - Assessment of patient compliance with protocol
  - Summary of patient and clinical staff assessment of the Theranos System and the Client Solutions team via end-of-study surveys
- ∞ Conclusions
  - o General
  - Technical
  - o Economic

## Introduction to Theranos:

Accurately, rapidly, and effectively profiling the efficacy dynamics of a therapy in clinical studies is an unmet need that has long challenged the conventional blood testing infrastructure.

Theranos has demonstrated in clinical studies that more frequent longitudinal time-series measurements on fresh whole blood samples with a multiplexed platform that eliminates the noise (and inability to accurately characterize very broad dynamic ranges) of conventional tests is imperative to effectively characterizing physiological changes and the efficacy of any intervention.

Theranos' wirelessly integrated data analytical system allows for 'baseline' profiles of pathway dynamics to be created and updated automatically as data is generated in the field. If needed, analyte selection or frequency of sampling can be adjusted at any time during the study based on the data coming in.

In future studies within a given indication, the data analytical infrastructure can be used for predictive modeling wherein new patient data can be indexed against the stored baseline profiles for earlier reads on efficacy dynamics and dose-response.

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# **Background on Theranos Studies:**

Every day gained in getting a new brand to market can be measured in millions of dollars.

Time is a major factor of cost of development of a new drug. For years the pharmaceutical industry has worked to drive every day possible out of the development process, and has reached a point where the physical limitations around the timelines for statistically significant data acquisition primarily determine the time to market.

Theranos Systems revolutionize those timeline constraints by enabling instant access to higher quality data and exponentially faster reads on efficacy and safety dynamics from the initiation of clinical trials. In doing so, Theranos is laying the foundation of a new growth model for pharma.

Theranos Systems radically impact revenues and growth on new and existing drugs in ways that were previously not possible:

- Faster approvals and studies Immediate access to results enables immediate decision making and planning; early reads on efficacy dynamics and dose optimization for subpopulations through more comprehensive longitudinal PK/PD profiling
- Reimbursement and differentiation Concrete reads on efficacy dynamics and visibility into mechanisms of action to optimize compounds dynamically
- Rapid access to multiple markets pre and post-approval early reads on efficacy through trends in the change in rate of key markers allow for rapid label expansion
- Amelioration of safety concerns more accurate reads on actual pathway dynamics enable rapid optimization where beneficial and delineation of patient sub-populations

## **Economic Impact of Theranos Studies to Pharma:**

Based on Theranos' previous experience, predictive modeling and more comprehensive longitudinal profiling has resulted in the demonstration of meaningful dose-response and efficacy dynamics profiles in 6 month timeframes where the conventional infrastructure took two years and was still not able to generate hard correlations. An 18 month time-savings, not to mention the ability to gain insight into methods for optimization for label expansion, can conservatively be equated to hundreds of millions of dollars gained. With industry estimates at \$1-3M a day for the value of each day gained in time to market, even 6 months saved ranges between \$180M and \$540M in return on investment.

Equally, once the infrastructure has been implemented, future studies are requiring about 25% fewer patients, reducing the patient costs, number of sites required, assay development, reagent screening, and infrastructure costs for shipping and processing samples through ambulatory point-of-care monitoring.

Overall savings on 6 month trials once the data analytical infrastructure has been established have averaged 50% of the cost of running an equivalent trial through the conventional infrastructure, further saving millions of dollars. As the data analytical engine evolves after the first 6 month study, costs are further reduced in each follow-on study, covering the cost of Theranos infrastructure and units many times over.

Ultimately though, the greatest economic return on investment lies in the ability to expand percentage market ownership through visibility into pathway dynamics that enables rapid characterization of responder populations in ways previously not possible. This capability enables commercialization of 'targeted blockbusters' by redefining a company's historical success rate in realizing the target product profile of each drug once it hits the market.

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# **Angiogenesis Program Overview:**

The primary objective of the present program was to demonstrate the functionality of Theranos Systems in such a way that future studies could fully leverage the power of comprehensive longitudinal time-series profiling for rapid compound optimization and development.

For this program, Theranos was asked to develop multiplexed point-of-care assays for VEGF and PIGF for use in monitoring patient pharmacodynamic response to anti-angiogenesis therapies. Because the development of VEGFR2 in that multiplex was desirable as a tool for use in future studies, Theranos developed the assay and included it in the point-of-care multiplex.

In this program, Theranos validated not only functional equivalence, but superior performance specifications of the Theranos multiplex to each of the respective 'gold-standard' kits.

An Interim Report on Assay Development was submitted to Pfizer in Q2 '07 upon successful completion of assay development.

As planned for at the interim update meeting with Pfizer, the first patient began participating in the study in July of 2007. In order to fast-track the program timeline, Theranos contracted an independent site - Tennessee Oncology Center.

Enrollment of Sutent patients at this site was very slow; from the time patient screening began (early 2007) and after discussions with respective members of the Pfizer team, the protocol was revised several times to increase the frequency of monitoring but reduce the total number of patients and shorten the monitoring cycles per patient. Likewise, enrollment criteria were broadened to include patients on other therapies with whom trends in the relevant markers could also be profiled.

In doing so, statistical significance in meeting the study goals could still be ensured. Multiple IRB submissions were filed. Final IRB and Informed Consent Forms were included in two interim update reports sent to Pfizer.

#### Goals of Study:

- 1. Generate preliminary data on VEGF and PLGF trends in cancer patients while assessing the use of the Theranos System in the hands of clinicians and patients.
- 2. Obtain feedback and recommendations from clinical staff.
- 3. Assess the use of the Theranos System in the hands of ambulatory patients at home.
- 4. Assess the Ambulatory Bioinformatics Communications System<sup>1</sup> including the physician and patient web portals as well as the data reports generated.

# Study design:

Patient screening began in January 2007, once the final site was selected, enrollment began. In July of 2007, the first patient was enrolled in the trial. This trial consisted of very ill late-stage (4<sup>th</sup> line) cancer patients with various tumor types receiving a variety of therapies at the Sarah Cannon Research Center at Tennessee Oncology (TNONC) in Nashville, Tennessee. The patients in the study typically resided in very remote locations across the eastern US. Almost all patients were not computer literate, and most were from low income families, unable to afford private telephone service.

The Theranos angiogenesis monitoring system was evaluated for clinical efficacy and as a means of more accurately and effectively monitoring cancer therapy and the progression of solid

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<sup>&</sup>lt;sup>1</sup> The Ambulatory Bioinformatics Communication System (formerly known as ABCS) was rebranded as TheranOS, the Theranos Operating System.



tumor cancers from a mechanism-of-action perspective. 32 patients were enrolled. Various cycles of therapies were monitored as well as physical changes in tumor size.

Four of the patients retracted consent to the study, three of them due to family problems and one due to mental and physical instability. Thus, Theranos increased the targeted enrollment number to ensure that the goal of demonstrating performance across significantly significant patient numbers would be met. That goal has now been achieved. To realize the goal, some patients had extended (60 day) monitoring periods.

Since Theranos has the ability to continue monitoring patients under the existing IRB and given the power of some of the correlations which are becoming apparent, Theranos may continue monitoring those patients for an extended period of time.

Enrollment was unpredictable and slow. All installations and shipments completed for this study were done on-demand with less than 24 hours. As part of the installation procedure, Theranos' client solutions team has performed at-home installations and pick-ups for many weak patients.

For each patient, a total of up to 14 time points were collected during the month-long analysis period, 3-4 time points taken at the clinic and the other 10-11 time points taken in-home. Both finger-stick and venous samples were taken during each clinic visit, while only finger-stick samples were run in-home. The venous draw samples were run on the Theranos System in the clinic at the time of the draw; these samples were also processed so that the plasma and/or serum was analyzed using a reference method.

Venous samples were processed using reference methods and provide an archive of 41 anticoagulated plasma and serum samples which were frozen and have subsequently been analyzed at Theranos.

## **Theranos System Overview:**

The Theranos System is comprised of consumer-oriented readers, single-use cartridges containing assay chemistry and controls, and a data collection system that communicates through cellular networks with the instrument to provide assay protocols and to compute and display results.

The steps required of a new patient are to 1) take the machine out of the box and 2) plug it into a power source. The touch-screen then walks each patient through the process of poking his/her finger, depositing blood into the cartridge, and placing the cartridge in the reader drawer. The instrument then processes the assays and sends the data through the cellular network in real-time to a secure web-portal.

Theranos Systems allow for quantitative, multiplexed longitudinal time-series measurements to map correlations between the rate of change of blood-borne markers over time to surrogate and clinical end-points.

#### Specifications:

- Designed for at home use. Can also be used in physician's offices, ICU, and laboratories.
- Multiplexed measurement of biomarkers.
- Customizable for different/new assays on demand.
- Average 6 measurements per cartridge
- Serial measurements to comprehensively profile pharmacodynamic response through trends
- Runs fresh whole blood, plasma or serum samples

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- Finger-stick small sample size
- Mix and match selection of analytes on demand.
- Wide measurement range
  - o pg/mLl mg/mL (1 billion fold)
- High sensitivity
  - o 0.2 pg/mL (2 parts per 10-billion)
- ❖ Analyte Recovery: ~100 %
- ❖ System CV post-calibration (inter-intra reader, cartridge, and assay): < 10 %
- On-board chemistry controls
- Factory calibration (no user calibration)
- Wireless communication of results to appropriate user through cellular network
- Proprietary algorithms to interpret time trend results

The existence of a technology infrastructure for home, real-time blood monitoring allows collection of information which cannot be obtained using conventional blood testing scenarios:

- Small sample (finger-stick) + more frequent sampling of a small subset of analytes enables:
  - o Identification of appropriate analytes (greatly helped by more frequent sampling)
  - Earlier detection of efficacy and safety and acute problems so intervention (for example, dose modification or change in drug type) can be more effective
  - o Convenience of monitoring through-out a time-course before an event
- Higher sample integrity; real-time sample analysis on fresh whole blood on a standardized platform which can be deployed at any location (world-wide) eliminates assay inaccuracy associated with commercially available tests performed on samples which are "old" by the time they are analyzed.
  - Elimination of erroneous results (caused by analyte instability) and inherent errors in data and patient correlations (caused by processing data at various contract locations)





For this study, an instrument was deployed in the home of each patient; four others were installed at the Cancer Center.

Three assays were performed simultaneously in multiplex by the system on a finger-stick sample of fresh whole blood. The analytes were Vascular Endothelial Growth Factor (VEGF), soluble VEGF receptor R2 (sVEGFR2, usually referred to as VEGFR2) and Placental Growth Factor (PLGF). Each assay was controlled using within-cartridge control measurements.

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The system was calibrated at Theranos. Multiple cartridge lots were produced each with successively more clinically relevant specifications once samples were received from patients in the trial, as samples were not available during assay validation. Each lot was independently calibrated.

Traceability of calibration: Calibration is traced to authentic analytes dissolved at known concentrations in a plasma-like matrix. Calibration materials are prepared as mixed solutions of the three analytes. Assignment of calibrator concentrations is then made to values found for measurements of calibrators using reference assays.

#### System Performance Goals:

| Assay  | Reportable low pg/mL | Reportable high pg/mL | Precision CV, % |
|--------|----------------------|-----------------------|-----------------|
| VEGF   | 20                   | 10,000                | 10              |
| VEGFR2 | 150                  | 15,000                | 10              |
| PLGF   | 5                    | 1,000                 | 10              |

#### Assay ranges achieved:

The goals for each assay's dynamic range were achieved. Due to the inability to receive samples for calibration at the beginning of the studies, the upper limit of calibration for VEGF was restricted to 3,000 pg/mL in the first cartridge lots, but then extended<sup>2</sup> to 10,000 pg/mL. For early cartridge lots the PLGF assay lower limit of sensitivity was 50 pg/mL. Therefore, many early results for PLGF were out-of-range low ("OORL"). Lots produced after receiving samples for calibration have reportable ranges below 20 pg/mL.

#### Specificity:

The specificity of the assays depends on the pairs of antibodies chosen for each assay. In the first instance, we rely on the antibody vendor information. Selected pairs are known to have good specificity in ELISA assays. Key issues for these analytes are (1) the structural relationship of VEGF and (2) the fact that VEGF binds to sVEGFR2. We have shown that the Theranos assay system is not affected by the presence of VEGF and VEGFR2 and PLGF in the same samples. In many patients in this study, the drug Avastin is used. This drug is an antibody that binds to VEGF. It is obvious that ELISA assays for VEGF (and perhaps VEGFR2) using antibody pairs are likely to be interfered with by Avastin. As documented below, Theranos assays for VEGF and VEGFR2 appear to function with minimal interference from Avastin. In contrast, the selected reference assay for VEGF is strongly interfered by Avastin.

# Theranos System Performance:

# Assay accuracy:

Accuracy has been evaluated by analysis of clinical samples. Two sets of samples have been used: (1) A set of 12 serum samples from cancer patients (obtained from a commercial vendor), (2) 41 archived serum and plasma samples from this study. Because Avastin was used to treat many of the patients in the TNONC study and this antibody strongly interferes with the reference method, we used the commercially available samples for VEGF assay evaluation.

Twelve serum samples were assayed (singlicate) in the Theranos system and in duplicate for the reference method with the following results:

VEGF: y (Theranos) = 0.785 x (reference) + 95.2; R<sup>2</sup> = 0.99. Range 96 – 1985 pg/mL. One sample was rejected from the analysis giving very high results in the Theranos system and low

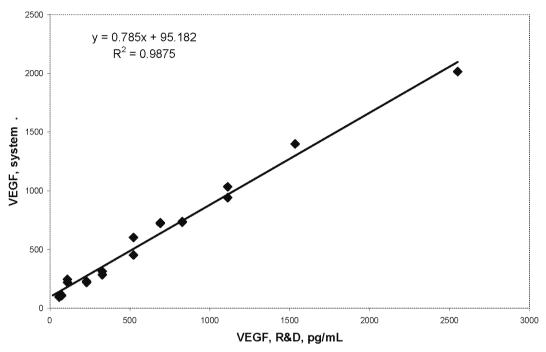
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<sup>&</sup>lt;sup>2</sup> All three assays have a linear dose-responses extending far above the highest calibrator used.



results in the reference assay. Based on the study data, it seems likely this patient was being treated with the drug Avastin, which interferes with the reference assay.

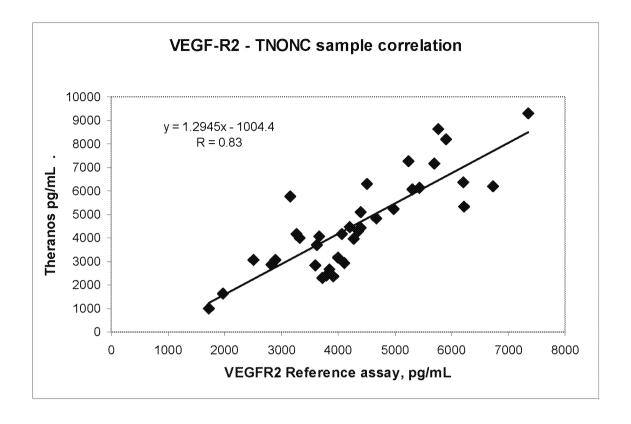
# Single cartridge clinical results



For VEGFR2, 39 TNONC samples were assayed in triplicate in the Theranos system and duplicate for the reference method. The results were: y (Theranos) =  $1.29 \, x$  (reference) + 1004; R = 0.83. Range  $1015 - 9285 \, pg/mL$ .

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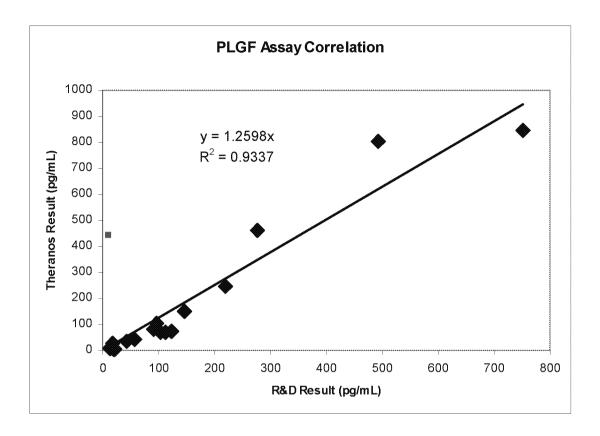


For the initial PLGF samples analyzed by Theranos in the field and with the reference method the results fell mostly in the undetectable range of both methods. Once the Theranos calibration was re-optimized, values became detectable from 5-17 pg/mL in the out-of-range-low venous samples sent to Theranos.

A significant correlation was achieved during validation on normal serum samples from twenty pregnant women assayed in quadruplicate. They were analyzed on both the Theranos system and the reference R&D Systems kit. The following results were obtained: y (Theranos) = 1.26\*x (R&D Systems); R = 0.96. The average within sample CV for the Theranos results was 9%. One sample (shown in pink) below gave discrepant results.

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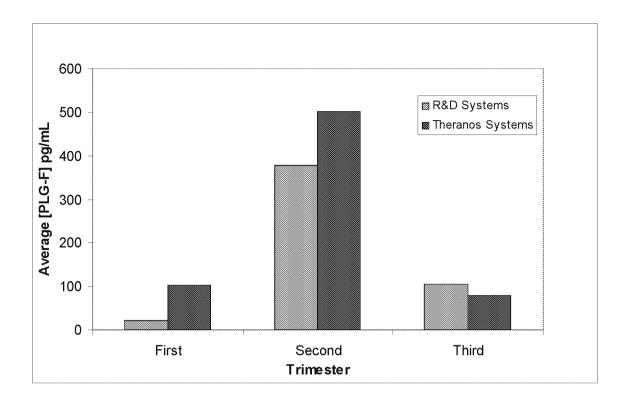




When the results for patients were segregated by trimester and averaged, the concordance shown below was found.

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# Effect of Avastin on the reference VEGF assay:

Comparison of reference and Theranos VEGF assay results for venous samples were not correlated. Many Theranos results were in the thousands of pg/mL where reference assay gave a low value. Since it was noted that many of the patients had been treated with Avastin which binds to VEGF, Theranos did a study of spike recovery for the reference method. VEGF (400 pg/mL) was added to each sample and the assay repeated. Results are shown below:

| Avastin | VEGF average, pg/mL    | VEGF average, pg/mL |
|---------|------------------------|---------------------|
| Present | Ref                    | Theranos            |
| Ν       | 149                    | 588                 |
| Υ       | 136                    | 8359                |
|         | \/"O" '\               |                     |
|         | VEGF spike recovery, % |                     |
| Ν       | 66.5                   |                     |
| Υ       | -1.3                   |                     |

It is evident that Avastin completely blocks the reference assay response. Presumably, Avastin binds at a site on VEGF close to or identical with that recognized by one of the antibodies used in the reference method. The reference assay thus responds only to free VEGF whereas the Theranos assay is not blocked and measures both Avastin-bound and free VEGF.

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# Assay precision:

#### Inter-Instrument Precision:

Venous samples from patients were run across four instruments.

| Assay  | Reportable low pg/mL | Reportable high pg/mL | Precision CV, % |
|--------|----------------------|-----------------------|-----------------|
| VEGF   | 20                   | 10,000                | 0.8             |
| VEGFR2 | 150                  | 15,000                | 7.3             |
| PLGF   | 5                    | 1,000                 | 9.2             |

Precision in comparison to available reference methods was evaluated during calibration. Singlicate measurements from six instruments were used next to commercially available 'gold-standards'. Theranos adjusted the target range after obtaining clinical samples. Due to the superior performance characteristics of Theranos' assay next to commercial standards, obvious variances are seen where the reference methods report OORL.

Single lot calibration data:

| Analyte        | Range (pg/mL)  | Average CV, % |
|----------------|----------------|---------------|
| VEGF (lot 3)   | 30 – 10,000    | 12.0          |
| VEGF (lot 1)   | 30 – 3,000     | 10.0          |
| VEGFR2 (lot 3) | 1,000 – 10,000 | 4.8           |
| VEGFR2 (lot 1) | 50 – 800       | 17.6          |
| PLGF (lot 3)   | 5 – 780        | 26.9          |
| PLGF (lot 1)   | 50 – 800       | 9.1           |

Precision was also measured by analysis of the 41 archived clinical samples in assays and for VEGF 12 commercial samples.

| Analyte Range (pg/mL) |                | Average CV, % |
|-----------------------|----------------|---------------|
| VEGF                  | 30 – 10,000    | 16.7          |
| VEGF <sup>3</sup>     | 96 – 1985      | 5.7           |
| VEGFR2                | 1,000 – 10,000 | 20.4          |
| PLGF                  | 5 – 780        | 28.7          |

#### Dilution linearity:

Data gathered during lot calibration.

| Recovery, % |
|-------------|
| (100)       |
| 102         |
| 95          |
| 105         |
| 109         |
| 105         |
| 101         |
|             |

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<sup>&</sup>lt;sup>3</sup> Commercial samples



| VEGFR2, pg/mL | Recovery, % |
|---------------|-------------|
| 10560         | (100)       |
| 7920          | 92.9        |
| 5280          | 100.9       |
| 3960          | 104.8       |
| 2640          | 97.7        |
| 1320          | 100.8       |

| PLGF, pg/mL | Recovery, % |  |
|-------------|-------------|--|
| 780         | 100.0       |  |
| 312         | 87.6        |  |
| 156         | 102.8       |  |
| 47          | 106.3       |  |
| 16          | 92.4        |  |
| 5           | 99.4        |  |

For all assays, recovery was close to 100 % in the reportable range.

# Limit of detection (LOD):

Data gathered during calibration. The LOD is defined at a 95 % confidence level.

| Analyte           | LOD, pg/mL |
|-------------------|------------|
| VEGF              | < 20       |
| VEGFR2            | < 200      |
| PLGF <sup>4</sup> | < 20       |

# Theranos Field Study:

The system has been deployed to patient's homes and the TNONC study clinic and has downloaded protocols and uploaded data wirelessly. Some patients used direct telephonic communications (POTs modems) if they were worried about cell reception. Data for every patient has been profiled on a secure, Pfizer-specific server.

## Field Performance Overview:

In this report we document results from:

- ∞ 27 patients (41% female and 59% male)
- $\infty$  13 cancer types
- ∞ 38 Instruments
  - o 27 instruments deployed to patients' homes
  - o 4 instruments deployed to the clinical site in Nashville, TN
  - 4 updated instruments to replace the readers at the clinical site such that the latest design revolution is deployed at the site

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<sup>&</sup>lt;sup>4</sup> Later stage cartridge lots



- 3 were used to replace malfunctioning readers in the field (2 at clinic one with communication issue, one mechanical due to user error; 1 at patient's home with mechanical issues from shipping)
- ∞ 445 cartridges (approximately 1300 assay results)
  - This number includes cartridges run in-house on archived plasma as well as results gathered in-field

Data acquisition has proven feasible in the home setting. There were instruments in the field operating in extreme temperature conditions (from very hot, no A/C to A/C turned to the maximum) as well as in very diverse locations (from RV's to log cabins in the middle of forests), in remote, difficult to reach areas where poor cellular reception is prevalent.

The instruments have been deployed across three states, including Kentucky, Pennsylvania and Tennessee. As mentioned, typical turnaround time for installation and patient at-home test was less than 24 hours without notice.

In monitoring this multiplex of analytes at far greater frequency than ever before, considerable patient-response variation can be seen across different sub-patient populations, therapies, and cancer types.

When we look at the <u>average</u> results from each patient and the variation seen for each patient, it is evident that the patients vary drastically:

|         | VEGF        | VEGFR2      | PLGF        |
|---------|-------------|-------------|-------------|
|         | Avg., pg/mL | Avg., pg/mL | Avg., pg/mL |
| Maximum | 13,584      | 6,317       | 410         |
| Minimum | 47.5        | 368         | 37.3        |

By evaluating sample statistics such as these, one can identify patients who are anomalous and who may benefit from therapy modification.

For example, of the 13 patients with colon cancer we see one subject with an average VEGF of 13,600 pg/mL and another with an average of 255 pg/mL whereas most of the patients had VEGF values quite closely clustered at 1000 - 5000 pg/mL. Similarly, we see some subjects who show very little variation in analyte values and others with wide variations presumably related to response (high or low) to therapy.

#### Trial Data:

The following raw trial data is included in the appended spreadsheet:

- 1. Clinic visit diagnostics (Patient characteristics and Clinical assay results)
- 2. Clinic visit pivot table (clinical results presented as a customizable pivot table)
- 3. Patient aggregate data (Compliance data, Result averages and CVs by patient and averages by cancer type)
- 4. All field analyte data results (from the Theranos system presented by patient in a filtered table format [sort-able])
- 5. Treatment data (drugs used and dosage)
- 6. Individual end-of-study results (patient evaluation of system)
- 7. Compilation and summary of end-of-study survey results
- 8. Data transmission statistics

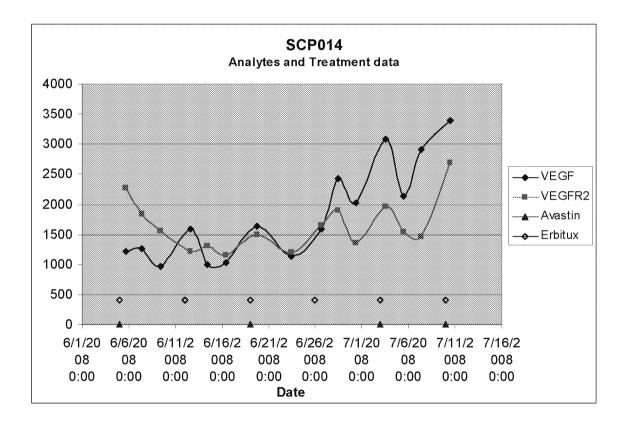
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## Evaluation of time course results from individual patients:

The study data demonstrates that in a larger, statistically controlled study, where the endpoint is directly proportional with patient outcome, e.g., a RECIST Score, a correlation between analyte dynamics and patient response to treatment would be generated.

To showcase the ability to profile predictive correlations between treatment and response profiles, we selected data from two patients -- 14 and 12. Due to patient 14's clinic schedule (first figure below), we were able to collect data following multiple infusion dates, allowing limited statistical analysis to be performed that correlates analyte levels with treatment administration. The cross-correlation function (second figure below) looking at VEGF and VEGFR2 blood levels for patient 14 shows a positive correlation at a cadence of 3 data points. This coincides with the patient's weekly clinic visits during which the patient receives the Avastin infusions.

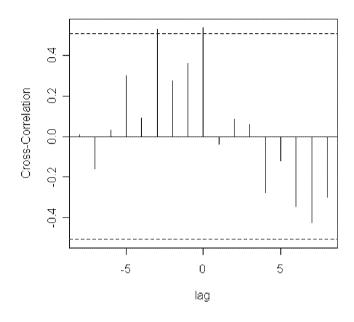


The change in rate of the parameters can be correlated to progress, seen again below in a correlation plot:

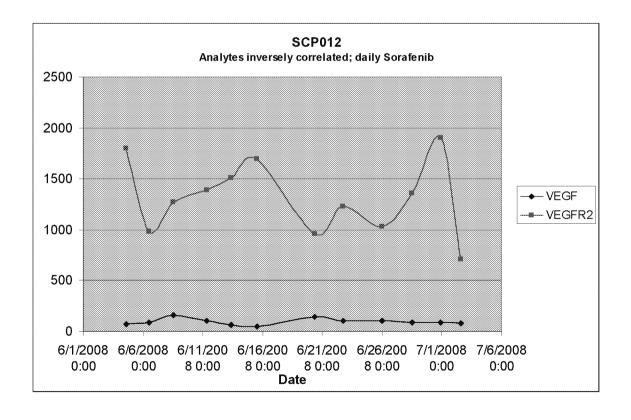
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# tnonc14.vegf & tnonc14.vegfr2



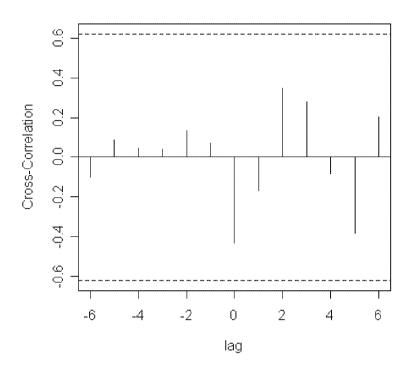
For patient 12 (first figure below), we observe an inverse correlation between VEGF and VEGFR2 blood levels. This suggests that the blood analytes behave differently with different drug treatments, pointing at distinct pathways of drug activity (second figure below).



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# tnonc12.vegf & tnonc12.vegfr2



For most patients analyzed, the sample size and sample numbers did not provide sufficient statistical power to derive a statistically significant conclusion but some clinical endpoint measurements were accessible to correlate analyte vectors and their rates of change with time to the patient's progression and response to treatment.

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# Patient average VEGF and VEGFR2 data by cancer type:

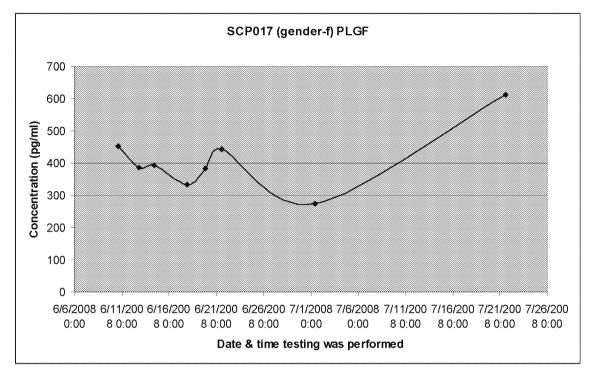
| Patient ID | Cancer type                       | Main<br>Treatment | Average VEGF (pg/ml) | Average<br>VEGFR2<br>(pg/ml) |
|------------|-----------------------------------|-------------------|----------------------|------------------------------|
|            | Adenocarcinoma                    | Sutent            | 47.5                 | 2592                         |
|            | Breast Cancer                     | Avastin           | 2082                 | 2662                         |
|            | Breast Cancer                     | Avastin           | 2055                 | 3040                         |
|            | Breast Cancer                     | Sorafenib         | 98                   | 1863                         |
|            | Colorectal Cancer                 | Avastin           | 4677                 | 3646                         |
|            | Colorectal Cancer                 | Sorafenib         | 1093                 | 4863                         |
|            | Colorectal Cancer                 | Sorafenib         | 3612                 | 5658                         |
|            | Colorectal Cancer                 | Sutent            | 72                   | 2798                         |
|            | Colorectal Cancer                 | Avastin           | 3860                 | 2350                         |
|            | Colorectal Cancer                 | Avastin           | 1840                 | 368                          |
|            | Colorectal Cancer                 | Avastin           | Patient dropped      | N/A                          |
|            | Colorectal Cancer                 | Avastin           | 1826                 | 1634                         |
|            | Colorectal Cancer                 | N/A               | Patient dropped      | N/A                          |
|            | Colorectal Cancer                 | Avastin           | 3006                 | 2143                         |
|            | Colorectal Cancer                 | Avastin           | 13584                | 5463                         |
|            | Colorectal Cancer                 | Sorafenib         | 255                  | 1540                         |
|            | Colorectal Cancer                 | Sorafenib         | 1274                 | 6317                         |
|            | Esophageal Cancer                 | Avastin           | 3145                 | 2260                         |
|            | Gastrointestinal Stromal<br>Tumor | Sutent            | 889                  | 2424                         |
|            | Liver Cancer                      | Sorafenib         | 96                   | 1253                         |
|            | Lung Cancer                       | Avastin           | 3947                 | 2111                         |
|            | Melanoma                          | Avastin           | 5399                 | 3294                         |
|            | Neuroendocrine carcinoma          | N/A               | Patient dropped      | N/A                          |
|            | Ovarian Cancer                    | Sorafenib         | Patient dropped      | N/A                          |
|            | Renal Cell Carcinoma              | Sutent            | 368                  | 883                          |
|            | Renal Cell Carcinoma              | Avastin           | 2316                 | 1057                         |
|            | Renal Cell Carcinoma              | Avastin           | 3159                 | 1911                         |
|            | Renal Cell Carcinoma              | Avastin           | 3908                 | 770                          |
|            | Renal Cell Carcinoma              | Avastin           | 3031                 | 1068                         |
|            | Tongue Cancer                     | Avastin           | 1457                 | 3074                         |
|            | Unknown Primary                   | Avastin           | 3099                 | 2980                         |

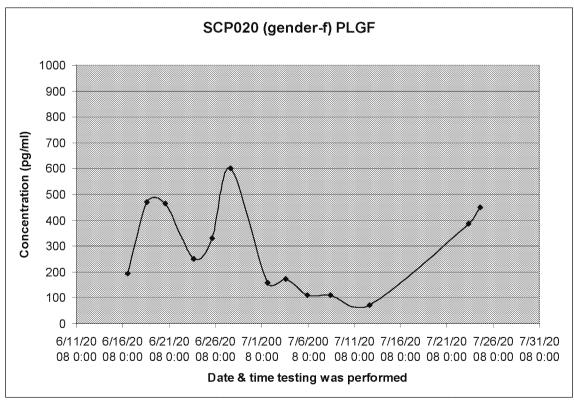
As referenced, patients dropped out of the study for various reasons; therefore average values are not statistically significant for them.

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For the patients in whom PLGF is consistently detectable we selected plots as shown below.





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Patient monitoring times and quality of life by gender:

| r adent monit   | oring times and quality of life by ge | iluei. |   | T  |
|---|---------------------------------------|--------|---|--|
|   |                                       |        | Time of day<br>when home<br>monitoring<br>was performed | Quality of life (as<br>measured by on-<br>screen survey) |
| Patient ID  | Cancer type                           | Gender | (on average)*   | (on average)*  |
|   |                                       | r      |   | N/A (Survey was not yet                                  |
|   | Adenocarcinoma                        | f      | Morning   | deployed)  |
|   | Breast Cancer                         | f      | Afternoon   | 7  |
|   | Breast Cancer                         | f      | Evening   | 8  |
|   | Breast Cancer                         | f      | Late Evening  | 7  |
|   | Colorectal Cancer                     | f      | Noon-afternoon  | 8  |
|   | Colorectal Cancer                     | f      | Afternoon   | 10   |
|   |                                       | _      | Afternoon-  |  |
|   | Colorectal Cancer                     | f      | Evening   | not yet available  |
|   | Colorectal Cancer                     | f      | Morning   | N/A (Survey was not yet deployed)                        |
|   | Lung Cancer                           | f      | Evening   | 9  |
|   | Ovarian Cancer                        | f      | N/A   | N/A  |
|   | Renal Cell Carcinoma                  | f      | Afternoon   | 6  |
|   | Unknown Primary                       | f      | Afternoon   | 9  |
|   | Colorectal Cancer                     | m      | Evening   | 7  |
|   | Colorectal Cancer                     | m      | Late Evening  | 7  |
|   | Colorectal Cancer                     | m      | N/A   | 8  |
|   | Colorectal Cancer                     | m      | Morning   | 7  |
|   | Colorectal Cancer                     | m      | N/A   | N/A  |
|   | Colorectal Cancer                     |        | Evening   | 8  |
|   | Colorectal Cancer                     | m      | Afternoon   |  |
|   |                                       | m      | <del></del>   | not yet available  |
|   | Colorectal Cancer                     | m      | Afternoon   |  |
|   | Colorectal Cancer                     | m      | Evening   | not yet available  |
|   | Esophageal Cancer                     | m      | Morning   | 8  |
|   | Gastrointestinal Stromal Tumor        | m      | Morning   | not yet available  |
|   | Liver Cancer                          | m      | Afternoon   | 10   |
|   | Melanoma                              | m      | Morning   | 9  |
|   | Neuroendocrine carcinoma              | m      | N/A   | N/A  |
|   | Renal Cell Carcinoma                  | m      | Noon-afternoon  | 10   |
|   | Renal Cell Carcinoma                  | m      | Morning   | 9  |
|   | Renal Cell Carcinoma                  | m      | Evening   | 10   |
|   | Renal Cell Carcinoma                  | m      | Evening   | 7  |
|   | Tongue Cancer                         | m      | Afternoon   | 5  |
| * Actual time for each test point and diurnal variations of quality of life can be found online |                                       |        |   |  |

Patient compliance with optional on-screen questionnaire was approximately 86% (this number was calculated before the end of the study, therefore final compliance figures may change).

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Patient clinical visit data by age:

| Patient<br>ID | Race                | Smoking Status                                | Alcohol<br>Consumption | Age | Weight (pounds) |
|---------------|---------------------|---|------------------------|-----|-----------------|
|               | Caucasian           | does not smoke now, positive history          | None                   | 36  | 179             |
|               | Caucasian           | never smoked                                  | monthly or less        | 45  | 165             |
|               | Caucasian           | Smoke daily                                   | None                   | 45  | 181             |
|               | Caucasian           | never smoked                                  | None                   | 46  | 213             |
|               | Caucasian           | smoke occasionally                            | None                   | 46  | 180             |
|               | Caucasian           | never smoked                                  | monthly or less        | 49  | 194             |
|               | Caucasian           | smoke occasionally                            | monthly or less        | 49  | 167             |
|               | Caucasian           | does not smoke now, positive history          | None                   | 53  | 190             |
|               | Caucasian           | does not smoke now, positive history          | None                   | 53  | 174             |
|               | Caucasian           | smoke occasionally                            | None                   | 57  | 262             |
|               | Caucasian           | does not smoke now, positive history          | None                   | 61  | 172             |
|               | African             | , ,   |                        |     |                 |
|               | American            | never smoked                                  | None                   | 62  | 167             |
|               | Caucasian           | never smoked                                  | None                   | 63  | 221             |
|               | Caucasian           | does not smoke now, positive history          | monthly or less        | 63  | 305             |
|               | Caucasian           | infrequent attempts (never developed a habit) | Every day              | 64  | 200             |
|               | Caucasian           | never smoked                                  | Every day              | 65  | 252             |
|               | Caucasian           | does not smoke now, positive history          | monthly or less        | 66  | 160             |
|               | Caucasian           | smoke occasionally                            | monthly or less        | 66  | 198             |
|               | Caucasian           | never smoked                                  | monthly or less        | 68  | 163             |
|               | Caucasian           | does not smoke now, positive history          | Every day              | 69  | 112             |
|               | Caucasian           | never smoked                                  | monthly or less        | 71  | 230             |
|               | Caucasian           | never smoked                                  | None                   | 72  | 101             |
|               | Caucasian           | never smoked                                  | None                   | 73  | 132             |
|               | Caucasian           | does not smoke now, positive history          | None                   | 73  | 134.5           |
|               | Caucasian           | does not smoke now, positive history          | None                   | 77  | 184             |
|               | Caucasian           | does not smoke now, positive history          | monthly or less        | 78  | 217.5           |
|               | African<br>American | never smoked                                  | None                   | 82  | 178             |
|               | Caucasian           | never smoked                                  | None                   | 83  | 182             |

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Sample of patient clinical blood work by patient ID:

|            | A 0/                  | Avg.          | A T-4-1                 | Avg.           | A           |
|------------|-----------------------|---------------|-------------------------|----------------|-------------|
| Patient ID | Avg. %<br>Lymphocytes | Heart<br>Rate | Avg. Total<br>Bilirubin | Systolic<br>BP | Avg.<br>RBC |
|            | 33.4                  | 67.7          | 0.7                     | 129.3          | 3.2         |
|            | 34.1                  | 55.0          | 0.3                     | 161.0          | 4.3         |
|            | 27.8                  | 64.7          | 0.5                     | 144.7          | 3.2         |
|            | 36.4                  | 75.0          | 0.2                     | 127.5          | 3.9         |
|            | 29.5                  | 100.7         | 0.3                     | 112.7          | 4.3         |
|            | 24.0                  | 73.0          | 0.3                     | 131.3          | 4.4         |
|            | 23.7                  | 84.0          | 0.4                     | 124.0          | 5.1         |
|            | 25.0                  | 71.5          | 0.7                     | 133.0          | 4.5         |
|            | 45.3                  | 74.3          | 0.9                     | 137.8          | 4.5         |
|            | 28.6                  | 82.0          | 0.6                     | 135.0          | 4.8         |
|            | 28.3                  | 75.5          | 0.7                     | 122.0          | 4.0         |
|            | 31.1                  | 72.0          | 0.7                     | 137.0          | 4.2         |
|            | 40.2                  | 81.5          | 0.4                     | 125.3          | 4.0         |
|            | 35.4                  | 78.3          | 0.3                     | 147.0          | 5.0         |
|            | 18.0                  | 75.3          | 0.3                     | 131.3          | 4.9         |
|            | 20.7                  | 89.3          | 0.4                     | 114.0          | 4.2         |
|            | 23.4                  | 70.0          | 0.3                     | 133.0          | 4.8         |
|            | 17.9                  | 60.7          | 0.4                     | 146.0          | 3.7         |
|            | 36.5                  | 91.0          | 0.4                     | 130.0          | 4.8         |
|            | 23.5                  | 93.5          | 0.7                     | 123.0          | 4.0         |
|            | 26.3                  | 107.7         | 0.7                     | 119.7          | 4.7         |
|            | 18.8                  | 83.0          | 0.7                     | 139.0          | 3.7         |
|            | 33.5                  | 94.0          | 0.3                     | 143.0          | 5.2         |
|            | 34.6                  | 110.0         | 0.4                     | 125.0          | 3.7         |
|            | 9.5                   | 70.0          | 0.7                     | 119.0          | 3.7         |
|            | 21.2                  | 98.0          | 0.8                     | 125.7          | 5.2         |
|            | 32.6                  | 90.5          | 0.6                     | 122.8          | 5.1         |
|            | 42.3                  | 72.0          | 0.4                     | 137.0          | 3.7         |
|            | 16.7                  | 70.0          | 0.4                     | 145.0          | 4.3         |

All individual patient data was profiled as it was generated on the Pfizer-specific secure portal at <a href="https://www.theranos.com">www.theranos.com</a>; raw data can also be found in the attached excel spreadsheet.

# Server and Data Transmission

Approximately 361 cartridge results and 203 optional home surveys from the field were successfully transmitted to the Theranos servers. There were less than 5% transmission errors that required the readers to either retry sending the data or wait until they had a better connection to send the data. All data gathered in the field was transmitted to the Theranos servers. For the first two patients, on-screen surveys were not available. The number of surveys received is smaller than the number of cartridge runs due to the above as well as patients filling only one survey for each of their clinic visits (even though they ran two cartridges per visit). Once surveys became available, each cartridge run also asked the user to complete an optional quality of life survey and compliance was very good.

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| Data distribution by transmission pathway to date |              |                        |  |  |  |  |
|---|--------------|------------------------|--|--|--|--|
| Direct Internet Connection                        | Wireless-GSM | Traditional Phone line |  |  |  |  |
| 5.6 %   | 90.7%        | 3.7 %                  |  |  |  |  |

The only problem encountered with using GSM wireless phone technology was poor signal. The main reasons for poor cellular reception were: dense foliage, metal roofs and poor signal quality due to remote location. In one location there was no cellular coverage at all; therefore the reader used the standard telephone line in order to connect to our servers and report data as it was gathered. All of this patient's logs were received by Theranos servers. In future studies, multiple network providers would be contracted for these areas.

# Overall performance of the Theranos System based on Customer Care log:

The customer care line was available to patients 24 hours a day 7 days a week over the course of the entire study (July 07 to October 08). All calls were addressed professionally and all issues were resolved quickly, taking care to minimize the impact on patients and clinical staff.

The types of calls for which patients used the Customer Care line:

- Patient running low on supplies the solution was to simply ship more of the needed supplies with overnight delivery to make sure patient had enough for the upcoming home tests.
- Patient not knowing how to turn machine on the solution was to advise the patient over the phone on the procedures outlined in the setup sheet they received and to make sure they have the instrument up and running.
- Patient calling about scheduling an instrument pickup solution was to schedule one of our representatives to pick up the machine or alternatively to have FedEx pick up the reader if patient was able to place it in the shipping container themselves.
- Patient called about blood transfer question the solution was to advise the patient to leave the blood transfer device on a flat surface. If this solution was not sufficient, a new batch was shipped to make sure no capillary manufacturer defects were at fault.
- Patient called about instrument not recognizing cartridge the solution was to ask patient to re-try and call back if problem persisted. The suspicion was that due to poor cellular signal the reader was unable to communicate, and by re-trying it would perform appropriately. There were no subsequent calls from patient.
- Patient called about instrument not being ready due to temperature the solution was to ask patient to move reader away from A/C units and possible air currents. Patients had moved readers from initial installation location (one moved it to his RV, another into a really hot room) and the temperature extremes affected the readers' ability to maintain desired temperature. The Theranos readers are engineered to control temperature to eliminate variability associated with conventional assays.

The majority of systems deployed in the field performed their duties throughout the entire length of the patient monitoring schedule. One instrument had mechanical issues due to being misused; this happened during new personnel training at TNONC. The instrument was promptly replaced with a new instrument. Another failure occurred due to the instrument being damaged in shipping. Although it performed its functions properly for the majority of the patient's schedule it eventually malfunctioned and was also promptly (~24 hours) replaced. Yet another issue was related to the cellular carrier not identifying the instrument. To expedite the process and assure that the clinic

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was adequately supplied it was decided to replace that instrument with one that was known to work. The problem was later resolved off-line.

### Patient Compliance with protocol:

It is hard to estimate the patient compliance with the exact protocol due to the factors out of Theranos' control. In many instances patients re-scheduled their clinic visits and the new appointments were not communicated to us. At the onset of each patient's home monitoring they were provided with a tentative schedule which in many cases changed due to patient's need to travel or inability to keep scheduled appointments. With this in mind, we estimate that patient compliance with protocol was still very good, at approximately 96 % (measured as 80-120% of expected testing completed and received). Given the missing information, a much more accurate derivation would be possible.

#### Theranos System Assessment by Patients and Clinical Staff:

Patient end of study surveys were sent out to all participants. To date, 17 responses were collected from patients.

Summary of patients' assessment of the Theranos system:

- 88% of patients surveyed found the Theranos System easy to use; no patients found it "very hard" to use.
- 76% of patients found the written instructions to be very informative, with clear directions;
  12% did not read instructions
- 91% of patients scored the training given by their Theranos representative either a 9 or 10 (10 being very good training)
- 76% of patients found the Theranos System takes little time to use (scores between 1 and 4 were tallied, with 1 = very little time and 10 = a lot of time)
- 100% of patients found the optional touch screen survey on the Theranos System easy to use, giving scores of either 8, 9 or 10 (10 = easy to use, 1 = hard to use).
- On a scale of 10 to 1 (10 = least painful, 1 = most painful), only one patient gave the blood drawing experience a score of less than 6. 59% felt almost no pain, scoring either a 9 or 10.
- 100% of the patients that responded to the survey gave Theranos Customer Support an excellent or very good rating
- For the majority of patients, the Theranos System worked very well. The major ways of solving the questions patients had were figuring it out on their own or calling the Theranos Customer Care line.
- In the follow-up survey, 100% of patients that responded said they received excellent or very good technical support over the duration of the study.
- Most patients said they prefer monitoring from home (scored 8 through 10) using the Theranos System; 25% were indecisive (scored 4 to 6) when asked whether they prefer going to the clinic or using the Theranos System; only two patients would rather monitor at the clinic.

From the interactions with clinical staff at Tennessee Oncology, the system was:

- 1. well received and
- 2. the client solutions team made a very positive impact on the clinical staff and patients through promptitude and professionalism.

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# Conclusions:

#### General:

- The Theranos System performed with superior performance to reference assays while running in a complex ambulatory environment.
- 2. The existing Theranos support infrastructure enables on-demand home installation and patient training in extremely rural areas.
- 3. Patients preferred ambulatory monitoring to clinic visits and liked using the Theranos System.
- 4. Non-computer literate patients had no issues using the Theranos System.

#### Technical:

- 5. Inter-system accuracy is excellent and was demonstrated on a platform with superior performance specifications to reference methods.
- 6. Calibrations were updated with access to samples from the trial.
- 7. Good correlations were seen to various commercially available gold-standards.
- 8. Avastin does not block the Theranos assay.
- 9. The Theranos System can measure VEGF both free and bound to VEGFR2 and Avastin to better quantify dose-response.

#### Economic:

- 10. This 15 month study demonstrated the robust functionality of Theranos Systems. With this validation data, the technology can be applied to significantly cut costs and bring compounds to market faster:
- 11. More frequent sampling enabled better characterization of longitudinal time-series profiles of angiogenesis protein panels. More accurate insight of the change in rate of those panels over time enables significantly faster and earlier reads on efficacy dynamics.
  - a. See efficacy dynamics trends and correlation to end-points in patient time-course profiles on the Pfizer web-portal at <a href="https://www.theranos.com">www.theranos.com</a>.
- 12. Response profiles were seen in this study over 30 day intervals. Historically, these types of correlations have taken up to a couple years to demonstrate, or in some cases, were previously not demonstrable. This time gained facilitates rapid data generation for additions to a compendia and rapid label expansion of existing drugs. Equally, this approach can be used to fast-track approvals of key compounds and at the same time better optimize those compounds with better visibility to achieve the target product profiles.
  - One of Theranos' pharma partners is publishing a report which estimates the increased time to market is valued at \$1M per day – making every month quite substantial.
- 13. Through Theranos Systems, Pfizer will be able to reduce the number of sites, eliminate shipping costs for samples, processing costs, and analytical costs. Based on historical data, implementation of these systems will enable Pfizer to achieve ~50% cost savings over current study spending (previously demonstrated to be \$15M of a \$30M study budget). Equally, through better insight into pathway dynamics, Theranos is demonstrating the ability to reduce the number of patients required to show statistical significance in future studies by 30-50%.

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